There are many causes of hypercalcemia but the following three are the most common: primary hyperparathyroidism, neoplasm and sarcoidosis. In primary hyperparathyroidism, hypercalcemia is associated with circulating parathyroid hormone levels in the high or high-normal range and elevated urinary secretion of adenosine 3′:5′-cyclic phosphate. A subnormal serum albumin concentration is a key feature of the hypercalcemia due to neoplasm; 1,25-(OH)2-D_3 levels are usually elevated. The serum chloride level is low in some patients with hypercalcemia due to malignancy. In sarcoidosis, hypercalcemia is associated with increased 1,25-(OH) 2-D_3 and serum angiotensin-converting enzyme levels; the parathyroid hormone concentration is normal. Thus, the triad of hypercalcemia, elevated serum angiotensin-converting enzyme and increased 1,25-dihydroxyvitamin D_3 strongly favor sarcoidosis as the cause of hypercalcemia.

Once the diagnosis of sarcoidosis is established, the treatment is relatively straightforward. I usually give 20 to 40 mg of prednisone daily in a single dose. For patients with severe hypercalcemia, I prefer a higher dosage—60 to 80 mg—of prednisone a day. The dose is then gradually reduced to a maintenance level of about 10 mg daily. An alternate-day regimen can be used effectively.

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Respiratory Muscle Fatigue

MUSCLE FATIGUE is defined as the inability to sustain a required force. The respiratory muscles behave like other skeletal muscles and fatigue develops when they are subjected to excessive loads. Muscle fatigue results from contractile failure within muscle fibers, rather than from impaired neuromuscular transmission or central nervous system fatigue. In addition to the treatment of underlying lung disease, the management of respiratory failure requires that attention be directed to the ventilatory pump itself. Factors that impair muscle contractility must be corrected. These include low cardiac output, acidosis, hypoxemia, hypercapnia and low serum levels of potassium, magnesium and phosphorus. In addition, other methods have been suggested to improve and optimize ventilatory muscle function and may be valuable both in acute conditions and for long-term benefit. These include drugs such as the methylxanthines, ventilatory muscle rest, ventilatory muscle training and nutritional supplementation.

Methylxanthines. Apart from a central stimulant effect, it is now clear that theophylline increases the contractile tension of skeletal muscle. The mechanism may be related to increased calcium release from the sarcoplasmic reticulum. Still controversial is whether the degree of enhanced contractility of the diaphragm is enough to avert respiratory failure or to provide significant clinical improvement in respiratory muscle function.

Ventilatory muscle rest. It has been suggested that chronic fatigue occurs in overloaded ventilatory muscles, leading ultimately to respiratory failure. In nonrespiratory skeletal muscle, recovery from fatigue may take several hours to days, and it has been proposed that resting the ventilatory muscle by the use of controlled mechanical ventilation may be beneficial in improving and strengthening contractility of the inspiratory muscles. Preliminary reports of nocturnal mechanical ventilation in hypercapnic patients with pulmonary and neuromuscular disease suggest that this method may be beneficial, but further control studies are necessary.

Nutrition. Undernutrition and weight loss impair ventilatory muscle strength and endurance, both of which predispose to and perpetuate respiratory failure. Nutritional repletion is important, but it must be remembered that high-calorie diets that contain a large percentage of carbohydrate produce larger quantities of carbon dioxide than do diets containing equicaloric proportions of carbohydrates and fats. Patients with impaired pulmonary function may have difficulty excreting this excess CO_2.

Ventilatory muscle training. Endurance training in general increases skeletal muscle endurance. For ventilatory muscles, there are two methods of training: one is the resistive method, in which the patient breathes at a normal rate through a high respiratory resistance, and the other is the hyperpneic method in which the patient does isocapnic hyperpnea for a prolonged period. Both these methods may improve ventilatory muscle endurance and in some studies have improved overall exercise tolerance in patients with chronic obstructive pulmonary disease. Further work is necessary to delineate the appropriate indications for training versus resting the ventilatory muscle.

The ventilatory pump is as vital to life as the heart. Understanding of the pathogenesis and reversal of ventilatory muscle fatigue is crucial to improving the management of respiratory failure.

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Continuous Monitoring of Mixed Venous Oxygen Saturation

CONTINUOUS MIXED VENOUS oxygen saturation ($S\bar{v}O_2$) monitoring is a research tool that has become commercially available for clinical use. The monitoring system consists of a light source and analyzer connected to fiber-optic bundles embedded within a pulmonary artery catheter. Oxyhemoglobin saturation is measured through the fiber-optic bundles by its predictable effect upon hemoglobin's light absorption.

$S\bar{v}O_2$ is determined by the balance between oxygen delivery and oxygen consumption. Oxygen delivery is dependent on both pulmonary and cardiovascular systems, while oxygen consumption is dependent on the clinical situation. With some exceptions, $S\bar{v}O_2$ generally functions as an indicator that overall cardiac and pulmonary function is adequate